IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF TEXAS
SHERMAN DIVISION

GLENDA MCCOY, and JOHN ROBERT MCCOY, themselves as PLAINTIFFS, and on behalf of decedents JON ANDREA ROBERTS, MICAYLA ROBERTS AND DYLAN ROBERTS, *Plaintiff,* *v.* *PFIZER, INC, and GREENSTONE PHARMACEUTICALS, LLC,* *Defendant.*	*Civil Action No. 4:09cv496* *JUDGE: MICHAEL H. SCHNEIDER*

DEFENDANTS' MOTION TO EXCLUDE
TESTIMONY AND REPORT OF GEORGE GLASS, M.D.

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Defendants Pfizer Inc and Greenstone Pharmaceuticals LLC ("Defendants") move to exclude the testimony of Dr. George Glass on the grounds that his opinions on general and specific causation are inadmissible under Federal Rules of Evidence 702 and 703.

INTRODUCTION

Plaintiffs allege that ingestion of the prescription antidepressant sertraline[1] caused their daughter, Jon Andrea Roberts ("Roberts"), to kill her husband and two children and then commit suicide. To prevail on any of their claims, Plaintiffs must prove both (i) that sertraline can cause people to commit homicide and suicide (general causation) and (ii) that sertraline, as opposed to another cause or set of causes, caused Roberts to commit homicide and suicide (specific causation). *See, e.g., In re Norplant Contraceptive Products Liability Litigation,* 215 F. Supp. 2d 795, 830 (E.D. Tex. 2002); *Owens v. American Home Prods. Corp.,* 2005 WL 1657036 at *2 (S.D. Tex. July 12, 2005) (collecting cases). Because general and specific medical causation are beyond the ken of laypersons, admissible expert opinion testimony is required to create a genuine issue of material fact for trial. *E.g., Guevara v. Ferrer,* 247 S.W.3d 662, 665-69 (Tex. 2007).

For these elements of their claims, Plaintiffs have designated Dr. George Glass, a Houston psychiatrist who describes himself as a "[d]octor of Medicine with specialization in Psychiatry and Substance Abuse, directed toward the diagnosis, treatment and rehabilitation of Alcoholism and Drug Abuse, as well as Chronic Pain, Stress Management and Post Traumatic

[1] Sertraline is the generic form of Zoloft®, a proprietary form of sertraline manufactured by Pfizer Inc. Sertraline is a member of the class of antidepressant medications known as selective serotonin reuptake inhibitors, or "SSRIs."

Stress." (*Curriculum Vitae* of G. Glass, MD, Ex. 1.) On the issue of general causation, Dr. Glass asserted in his report that "there is a vast body of medical literature supporting the link between SSRI's and bizarre suicidal, and or homicidal behavior." (Rpt. of G. Glass, MD at 9, Ex. 2.)

Beyond that *ipse dixit* assertion, however, Dr. Glass has identified no medical literature whatsoever that purports to have found, demonstrated, or scientifically established any causal relationship between ingestion of sertraline and suicide or homicide. Texas law is clear on the minimally sufficient kind, number and quality of scientific studies that a plaintiff's expert must adduce in support of medical causation opinions such as Dr. Glass's here. Because Dr. Glass has conceded that he cannot support his opinions with the required scientific data, his testimony must be excluded. In addition, Dr. Glass has completely disregarded the best available evidence on the question of whether SSRIs generally, and sertraline specifically, are associated with an increased risk of suicidality in adults.[2] In 2006, FDA compiled and analyzed placebo-controlled clinical trial data from hundreds of studies of modern antidepressants, including sertraline. The FDA analysis found that, for patients above age 24 (like Andrea Roberts) (i) SSRIs as a group are not associated with an increased risk of suicide, and (ii) that treatment with sertraline– the sole medication at issue in this case—is associated with a statistically significantly ***decreased*** risk of suicidality. Dr. Glass's "methodology" in arriving at his opinions in this case thus not only is devoid of the requisite scientific support under Texas law, but simply ignores the FDA

[2] The term "suicidality" encompasses all forms of suicidal behaviors, ranging from suicidal thoughts, to suicide attempts, to completed suicide.

analysis, as well as numerous other epidemiological studies that similarly find no increased risk of suicidality in adult patients.

Dr. Glass's specific causation opinion is similarly unscientific and unreliable. Dr. Glass did not review any of the available evidence concerning Roberts' behavior before or after she was first prescribed sertraline. Specifically, Dr. Glass has not read any of the fourteen depositions that have been taken of Roberts' family, friends and medical providers. His specific causation opinion, accordingly, is based on an incorrect and unreliable view of the facts, and amounts to nothing more than self-serving and fallacious *post hoc* reasoning that because Roberts behaved the way she did *after* she ingested sertraline, her behaviors were *caused* by sertraline. The facts Dr. Glass ignored, as shown below, demonstrate the inaccuracy and illogic of his reasoning. Finally, Dr. Glass's opinion that Pfizer attempted to "minimize side effects" and delay notifying FDA and physicians of facts concerning the risks of sertraline is based on literally no information about Pfizer or its actions, and is therefore pure speculation. [3]

[3] Because expert testimony is essential for Plaintiffs to establish causation, summary judgment should enter upon exclusion of Dr. Glass's opinions. *See Romo v. Ford Motor Co.*, No. Civ.A. B-10-66, 2011 WL 2836315, at *7-9 (S.D. Tex. June 24, 2011) (plaintiff's failure to designate expert on causation necessitated summary judgment in favor of defendant on product defect claim); *Renfro v. Hartford Underwriters Ins. Co.*, No. CIV. 3:06-CV-2052K, 2007 WL 2446281, at *2 (N.D. Tex. Aug. 29, 2007) (when plaintiff cannot carry burden of proof at trial without providing expert testimony on the issue of causation, and plaintiff failed to timely designate an expert, plaintiff is unable to raise a genuine issue of material fact on the issues of causation and summary judgment is appropriately granted); *Koenig v. Purdue Pharma Co.*, 435 F. Supp. 2d 551, 553-54 (N.D. Tex. 2006) (causation is an essential element in strict liability, breach of warranty, negligence, and misrepresentation claims and thus plaintiffs failure to proffer evidence showing causation requires summary judgment in favor of defendant); *Qualls v. State Farm Lloyds*, 226 F.R.D. 551, 557 & 559 (N.D. Tex. 2005) (when plaintiff's claims required expert testimony to prove causation, plaintiff's failure to designate an expert required summary judgment for defendant).

ARGUMENT

Federal Rule of Evidence 702 provides that qualified expert testimony on a scientific or technical matter may be admitted only if "(1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the principles and methods reliably to the facts of the case." Fed. R. Evid. 702. This rule incorporates the principles set forth in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993) and its progeny. Rule 702 requires the trial court to act as a gatekeeper, ensuring

> the reliability and relevancy of expert testimony. It is to make certain that an expert, whether basing testimony upon professional studies or personal experience, employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field.

Kumho Tire Co. Ltd. v. Carmichael, 526 U.S. 137, 152 (1999). In sum, "the party seeking to have the district court admit expert testimony must demonstrate that the expert's findings and conclusions are based on the scientific method, and, therefore, are reliable." *Moore v. Ashland Chem. Inc.*, 151 F.3d 269, 276 (5th Cir. 1998). The gatekeeping function "separates expert opinion evidence based on 'good grounds' from subjective speculation that masquerades as scientific knowledge." *Glastetter v. Novartis Pharm. Corp.*, 252 F.3d 986, 989 (8th Cir. 2001).

The Supreme Court has made clear that an expert testifying about scientific matters must provide more than "subjective belief or unsupported speculation." *Daubert*, 509 U.S. at 590. The "party seeking to have the district court admit expert testimony must demonstrate that the expert's findings and conclusions are based on the scientific method." *Moore*, 151 F.3d at 276.

I. DR. GLASS'S GENERAL CAUSATION OPINIONS ARE NOT BASED ON RELIABLE METHODOLOGY

A. Proper Methodology for Determining General Causation

Epidemiology is the scientific study of the incidence and causes of disease, including adverse effects of medicines and vaccines. *See* Reference Manual on Scientific Evidence 3d Ed. 551 (Fed. Jud. Ctr. 2011) ("Reference Manual") (Ex. 3). To quantify the increased risk of a particular effect that is ***associated with*** exposure to a particular medication (whether or not ***caused by*** the medicine itself),[4] scientists calculate a "relative risk" or "odds ratio." *See, e.g.*, *Daubert v. Merrell Dow Pharms., Inc.*, 43 F.3d 1311, 1320-21 (9th Cir. 1995), *cert. denied*, 516 U.S. 869 (1995):

> The strength of an association between exposure and disease can be stated as a relative risk (RR), odds ratio (OR), or attributable proportion of risk (APR). Each of these measurements of association examines the degree to which the risk of disease increases when individuals are exposed to an agent.
>
> A commonly used approach for expressing the association between an agent and disease is relative risk. It is defined as the ratio of the incidence of disease in exposed individuals compared to the incidence in unexposed individuals. Thus, it can be expressed algebraically as $RR = I_e / I_c$, [where] RR is the relative risk, I_e is the incidence of disease in the exposed population, and I_c is the incidence of disease in the control [*i.e.*, unexposed] population.

[4] The Reference Manual (at 619) defines "association" in this field of science as follows:

> Events are said to be associated when they occur more or less frequently together than one would expect by chance. Association does not necessarily imply a causal relationship. Events are said not to have an association when the agent (or independent variable) has no apparent effect on the incidence of a disease (the dependent variable). This corresponds to a relative risk of 1.0. A negative association means that the events occur less frequently together than one would expect by chance, thereby implying a preventive or protective role for the agent (e.g., vaccine).

Thus, as the Reference Manual explains, a relative risk of 1.5 would indicate that the risk of the adverse event at issue is one and a half times higher in the exposed group than in the unexposed group. This is called a "positive association," but it does not establish a causal relationship. A relative risk of 1.0 indicates that the risk is the same between groups, which is deemed "no association." A relative risk less than 1.0 means that the risk is less in exposed persons. This is called "a negative association, which could reflect a protective or curative effect of the agent on risk of the disease." Reference Manual at 566-69 & n.53 (citing judicial decisions explaining and applying principles of relative risk and odds ratio).[5]

As noted, establishment of an association is not sufficient to prove causation. Instead, after identifying a positive association, valid scientific methodology dictates that the association

[5] Any relative risk figure is only as valid as the study from which it is derived. Methodological flaws can produce erroneous or misleading results, and good scientists take measures to avoid such errors. *See* Reference Manual at 572-597. Similarly, even a valid relative risk figure only provides information about the particular relationship studied; for example, a relative risk of infection of 2 between two antibiotics may show that the risk of infection is twice as great on one than the other, but would not tell anything about whether either of them increases risk of infection, because there is no unexposed control group to permit comparison to the risk in untreated patients. *See* B. Spilker, Guide to Clinical Trials 62 (1991) (Ex. 4) (placebo control group "helps control for adverse events being attributed to a medicine when they result from spontaneous changes in the disease or from other causes," and "if an active medicine but not placebo is used in a clinical trial, there is no statistical test to demonstrate that active medicine was effective, regardless of the effect observed."); *see also Awad v. Merck & Co.*, 1999 WL 681389, *4-6 (S.D.N.Y. 1999) (epidemiological studies provided no reliable evidence of causation where placebo-controlled clinical trial showed "no evidence of a statistically significant difference in the incidence of [injury] among rubella vaccines compared with the placebo group" and two nonexperimental studies showed no difference between vaccinated and unvaccinated patients); *In re Hanford Nuclear Reser. Litig.*, 1998 WL 775340, *22 (E.D. Wash. 1998) (study lacking unexposed control group was unreliable evidence of increased risk) (Ex. 96); *Zwillinger v. Garfield Slope Hous. Corp.*, 1998 WL 623589, *15 (E.D.N.Y. 1998) (expert's testimony unreliable where, *inter alia*, his study did "not include any individuals who were not exposed").

be analyzed under established criteria to determine whether the association is causal. The proper analysis for determining causation is explained in the Reference Manual:

> In assessing causation, researchers first look for alternative explanations for the association, such as bias or confounding factors, which are discussed in Section IV, *supra*. Once this process is complete, researchers consider how guidelines for inferring causation from an association apply to the available evidence. . . . The factors that guide epidemiologists in making judgments about causation (and there is no threshold number that must exist) are
>
> 1. Temporal relationship,
> 2. Strength of the association,
> 3. Dose-response relationship,
> 4. Replication of the findings,
> 5. Biological plausibility (coherence with existing knowledge)
> 6. Consideration of alternative explanations,
> 7. Cessation of exposure,
> 8. Specificity of the association, and
> 9. Consistency with other knowledge.
>
> . . . These guidelines reflect criteria proposed by the U.S. Surgeon General in 1964 in assessing the relationship between smoking and lung cancer and expanded upon by Sir Austin Bradford Hill in 1965 and are often referred to as the Hill criteria or Hill factors.

Reference Manual at 598-600 (footnotes omitted). The Manual goes on to explain each factor's meaning and proper application. Tellingly, Dr. Glass could not even identify these criteria at his deposition. (Deposition of Dr. G. Glass ("Glass. Dep.") at 129:2-130:16, excerpts attached as Ex. 5.) As shown below, no reliable study establishes even an association between sertraline and homicide or suicide, so Dr. Glass could not validly proceed to applying the criteria to evaluate causation, even if he did know what they were.

B. Dr. Glass's Opinion that Sertraline Causes Homicide is Unscientific and Unreliable

Dr. Glass has not identified a scintilla of scientific support for the proposition that sertraline has the capacity to induce homicide in any individual or group of individuals. (*See* Glass Dep. at 237:3-11.) The starting point for any scientific evaluation of the proposition that a causal relationship exists between ingestion of a medication and a putative "side effect" known to manifest in the absence of exposure to the medication is scientific confirmation of at least a positive association (increase in risk) between the medication and the putative outcome. As explained above, such associations are determined in epidemiological studies. Absent epidemiological evidence of an association between a medication and an outcome of interest, there is no scientific basis to make the inferential leap that the medication, as opposed to other known and unknown non-drug causes of the outcome, is itself a cause of that outcome. The Fifth Circuit addressed this issue in *Brock v. Merrell Dow Pharms., Inc.*, 874 F.2d 307 (5th Cir. 1989) *modified by* 884 F.2d 166 (5th Cir. 1989).[6] In that case, the manufacturer of Bendectin appealed a jury verdict finding that Bendectin caused the plaintiffs' daughter to suffer birth defects. *Id.* at 308.

In analyzing whether the plaintiffs had presented sufficient evidence in support of general causation, the court noted that no published epidemiological study had found a statistically significant association between Bendectin and birth defects. *Id.* at 312 ("No published epidemiological study has found a statistically significant increased risk between exposure to

[6] Although *Brock* was decided before *Daubert*, courts have recognized its continuing validity under the *Daubert* standard. *See Kelley v. American Heyer-Schulte Corp.*, 957 F. Supp. 873, 878 (W.D. Tex. 1997).

Bendectin and birth defects."). Finding "the Brocks' failure to present statistically significant epidemiological proof that Bendectin causes [the injury at issue] to be fatal to their case," the court reversed the verdict in favor of the plaintiffs on the grounds that sufficient evidence had not been presented to establish general causation. 884 F.2d at 166; *see also Kelley v. American Heyer-Schulte Corp.*, 957 F. Supp. 873, 881 (W.D. Tex. 1997) (finding that general causation opinion should be excluded because epidemiologic studies were "not reasonably supportive of" the opinion.") As Dr. Glass admits, he cannot identify any study establishing even an association between sertraline and homicide. Accordingly, his opinion that sertraline caused Roberts to commit homicide is utterly unsupported and unreliable.

C. Dr. Glass's Opinion Lacks the Minimum Scientific Evidence Required Under Texas Law for Expert Testimony on General Causation

Dr. Glass's opinion also is unreliable and irrelevant because it is not based on scientific evidence sufficient to establish causation under *Merrell Dow Pharmaceuticals, Inc. v. Havner*, 953 S.W.2d 706 (Tex. 1997). To satisfy *Havner*, Dr. Glass must support his opinions with at least two reliable epidemiological studies establishing a statistically significant doubling of risk of homicide and suicide associated with use of sertraline. 953 S.W.2d at 718. Dr. Glass has admitted that he cannot identify any study finding a statistically significant doubling of risk for suicide or homicide associated with sertraline. (Glass Dep. at 148:5-11; 237:12-17.)

As the United States District Court for the Western District of Texas held in *Cano v. Everest Minerals Corp.*, 362 F. Supp. 2d 814, 822 (W.D. Tex. 2005), "*Havner* controls the issue of what evidence is required to establish causation in a toxic tort case and therefore what evidence is relevant." Accordingly, the *Cano* court found that expert opinion that will not pass muster under *Havner* should not be admitted under *Daubert*. *Id.* Although the United States

District Court for the Northern District of Texas reached a different conclusion in *Lofton v. McNeil Consumer & Specialty Pharmaceuticals*, 682 F. Supp. 2d 662, 668-69 (N.D. Tex. 2010), the *Cano* decision is better-reasoned. As the *Cano* court explained:

> If evidence is admissible under federal procedural law but fails to constitute "some evidence" under Texas substantive law, the Plaintiff's victory on the admissibility question would be a hollow one, as the evidence would be deemed insufficient as a matter of law to survive summary judgment. Moreover, whether expert testimony will assist the trier of fact is governed in part by whether the testimony is relevant to the plaintiff's burden of proof under the substantive law, and testimony that will not assist the trier of fact by advancing an element of the plaintiff's case should be excluded. *See Daubert v. Merrell Dow Pharms.*, 43 F.3d 1311, 1320 (9th Cir. 1995).[7]

362 F. Supp. 2d at 821-22. Thus, this Court should follow *Cano* and find that, because Dr. Glass's opinion cannot establish causation under Texas law, the opinion is irrelevant and unreliable.

D. Dr. Glass's Opinion is Unreliable Because He Ignored the Best Available Evidence Concerning Sertraline and Suicidality

1. The Most Reliable Evidence Establishes that Sertraline Reduces to the Risk of Suicidality in Adults

In epidemiology, health effects of medicinal compounds can be studied by experimental epidemiological studies, called "clinical trials," or by various nonexperimental techniques, such as "cohort" or "case-control" studies. *See, e.g.*, Reference Manual at 555-56. It is universally recognized that, because of their ability to control for potential bias and confounding through randomization, controlled clinical trials provide the most convincing evidence of drug effects.

[7] Like the *Havner* court, the Ninth Circuit in *Daubert* concluded that a relative risk of two or greater was necessary to prove causation because, as the court concluded, at least a doubling of risk is necessary to conclude that a medication more likely than not caused an adverse health outcome. 43 F.3d at 1320-21

See K. Rothman & S. Greenland, Modern Epidemiology 67-78 (1998) (explaining types of epidemiologic studies; "The scientific experiment is emblematic of scientific activity.") (Ex. 6); B. Spilker, Guide to Clinical Trials 53, 57 & Table 7.10 (1991) (of the various epidemiological study designs, the "randomized clinical trial (experimental study)" is the "most convincing design" and is the "only design that controls for unknown or unmeasurable confounders") (Ex. 4). Indeed, the Reference Manual for Scientific Evidence notes that "a randomized trial, clinical trial, or true experiment, is considered the gold standard for determining the relationship of an agent to a health outcome or adverse side effect." Reference Manual at 555.

In November 2006, FDA completed a definitive analysis of this type of "gold standard" evidence—hundreds of controlled clinical trials of modern antidepressants—to determine the relationship, if any, between antidepressants and suicidality. (*See* Stone and Jones, Clinical Review: Relationship Between Antidepressant Drugs and Suicidality in Adults (Nov. 17, 2006) ("Stone and Jones"), Ex. 7.) That analysis confirmed that (i) for individuals in Roberts' age-group (*i.e.*, over age 24), antidepressants as a group do not increase the risk of suicidal thoughts or behaviors, and (ii) across all analyses and age-groups, Zoloft is the safest antidepressant analyzed by FDA. Indeed, in Zoloft adult clinical trials, suicidal thoughts and actions occurred at a substantially ***lower*** rate in patients treated with Zoloft as compared with patients treated with placebo, the ***opposite*** of the relationship that would be observed if Zoloft caused additional acts or events in treated patients.

FDA analyzed data from double-blind, randomized, controlled clinical trials of sertraline and other antidepressants. (*See* Stone and Jones at 6 ("This review examines the relationship between antidepressant drugs and suicidality in adult subjects, as assessed within randomized,

placebo-controlled trials for various indications.").) Dr. Glass's report does not even mention FDA's analysis, much less offer any explanation how he can conclude, in direct opposition to FDA's findings based on "gold standard" evidence, that sertraline can cause suicide in patients like Ms. Roberts.

In its 2006 analysis, FDA consistently found, among several different analyses, that less suicidal thoughts and actions were reported in adult patients treated with antidepressants than in those treated with placebo. These results are expressed by a statistical measurement called the odds ratio, which is simply the ratio of the odds that a patient with suicidality was treated with a medication to the odds that such a patient was treated with an inactive sugar pill. An odds ratio of 1.0 thus indicates equivalent risk between drug and placebo, an odds ratio larger than 1.0 indicates increased risk in drug-treated patients, and an odds ratio less than 1.0 indicates decreased risk in drug-treated patients, compared to placebo. *See* Reference Manual at 568-69

FDA's analysis of suicidality in sertraline treated patients found a statistically significant odds ratio of 0.51, indicating that there was approximately ***half the risk*** of suicidal thoughts and actions in adult patients treated with sertraline as in patients given a placebo. (*Id*.) The sertraline-specific data for actual suicidal behaviors (excluding mere suicidal thoughts) were still more reassuring, with a statistically significant odds ratio of 0.25, indicating that ***one fourth*** as many suicidal behaviors occurred in Zoloft exposed adult patients. (*Id.* at 26, table 16.) FDA concluded based on these results that there is no increased risk of suicide for adult patients treated with antidepressants. For sertraline specifically, FDA concluded that "***the most consistent finding is an odds ratio for sertraline that is lower than for other drugs, both SSRI and non-SSRI***." (*Id.* at 39.)

As a result of these findings, FDA in May 2007 mandated revised labeling for all antidepressants reflecting the ***absence*** of suicide risk for patients above age 24:

> Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of Zoloft or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. ***Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older.***

(*See* U.S. Zoloft Labeling (June 2007) at 2576, Ex. 8 (emphasis added).)[8]

Dr. Glass admitted at deposition that he did not consider FDA's findings in forming his opinions. Incredibly, until he was shown FDA's report during his deposition, he did not even know what FDA's findings as to sertraline were:

> Q. Are you aware that there's a detailed report of FDA's analysis of randomized clinical trials of Zoloft and other antidepressants?
>
> A. I may have reviewed it in the past.
>
> Q. Did you review it in reference to this case?
>
> A. I don't believe so.
>
> Q. Do you have any recollection as to what the results were as to sertraline?
>
> A. Not specifically sertraline, no.

(Glass Dep. at 32:3-15.) Dr. Glass further admitted that he did not address the results of ***any*** clinical trials of sertraline in his report. (*Id.* at 33:7-10.)

[8] In his report, Dr. Glass misleadingly cites only FDA's mandated black box warning concerning children and adolescents in an apparent attempt to create a false impression that FDA may believe that antidepressants increase suicide risk in patients of all ages. (*See* Glass Rpt. at 7-8.)

In addition to ignoring the results of FDA's analysis of gold standard clinical trial evidence showing that sertraline is not associated with an increased risk of suicide, Dr. Glass also has totally disregarded a large body of epidemiological studies supporting the same conclusion. In fact, Dr. Glass admitted that he did not even conduct a literature review to determine what literature was available concerning sertraline and suicide. (*Id.* at 125:15-18.) Dr. Glass also did not cite in his report any literature published after 2006, and admitted that he made no attempt to determine whether there have been any publications in the past five years elucidating the relationship between antidepressants and suicide. (*Id.* at 125:19-126:14.)

In short, Dr. Glass, while claiming in *ipse dixit* fashion the existence of a "vast" body of supporting literature despite his inability to identify a single controlled study espousing anything remotely resembling his opinions, completely ignored the vast body of literature that actually does exist and that refutes his opinions. For example, in 2008, Barbui and colleagues conducted a meta-analysis of eight epidemiological studies involving more than 200,000 subjects to evaluate the relationship between antidepressants and suicidality. *See* C. Barbui et al. *Selective Serotonin Reuptake Inhibitors and Risk of Suicide: a Systematic Review of Observational Studies*. 180 Canadian Med. Assoc. J. 291, 291 (2009) (Ex. 9). Based on their meta-analysis, the authors concluded "[b]ased on data from observational studies, use of SSRIs may be associated with a ***reduced risk of suicide in adults*** with depression." *Id.* at 291 (emphasis added). As for sertraline specifically, the authors found an odds ratio for suicide attempt or completed suicide in adults of 0.46, indicating, similarly to FDA's analysis, that suicidality was decreased in sertraline-treated adults.[9] *Id.* at 296, Fig. 4. Dr. Glass testified that he had never even read this

[9] However, unlike in FDA's analysis, this finding was not statistically significant.

study. (Glass Dep. 237:18-238:3.) Dr. Glass also could not remember reading any of the studies that were combined for analysis in the *Barbui* study. (*Id.* at 240:5-16.)

There is a vast additional body of epidemiological studies evaluating the relationship between antidepressants and suicidality in adults. With the single exception discussed below, these studies find either no relationship or a decrease in risk of suicidality associated with sertraline therapy. (*See* Expert Rpt. of R. Gibbons, PhD, Ex 10.) Dr. Glass has ignored all of this evidence in rendering his opinions in this case, and did not even bother to read the report of Defendants' expert biostatistician, Dr. Gibbons, detailing the extensive literature on SSRIs and suicidality. (Glass Dep. 162:16-18.)

The United States District Court for the District of New Mexico addressed a strikingly similar situation in excluding a plaintiff's expert who opined that another SSRI, Prozac, caused plaintiff's decedent to murder his wife and then commit suicide. *See Rimbert v. Eli Lilly & Co.*, No 06-0874, 2009 WL 2208570 (D. N.M. Jul. 21, 2009). In words that could have been written to describe Dr. Glass's opinion in this case, the court noted:

> At the time she wrote her report, Dr. Jackson was aware of a body of published medical and scientific literature, including controlled clinical trials and other epidemiological studies, which supports the proposition that Prozac is not associated with suicidality, but she did not consider that literature in the formation of her opinions and report in this case. Additionally, when she wrote her report in this case, Dr. Jackson was aware that the FDA had reported to the public and to medical communities the results of its analysis of controlled clinical trials of antidepressants, including Prozac, and its conclusions that ingestion of antidepressants, including Prozac, creates no increased risk of suicidality in adults over age twenty four years of age and results in *decreased* risk of suicide in individuals over the age of sixty-five. . . . Nor did she examine the controlled clinical trial data examining the issue of whether Prozac causes suicide, despite being aware of its availability.

Id. at *13 (citations omitted).[10] After discussing these shortcomings, the court found the expert's general causation opinions unreliable because "where there is a large body of contrary epidemiological evidence, it is necessary to at least address it with evidence that is based on medically reliable and scientifically valid methodology . . . where epidemiology is available, it cannot be ignored. As the best evidence of general causation, it must be addressed." *Id.* at *14 (quoting *Norris v. Baxter Healthcare Corp.*, 397 F.3d 878, 882 (10th Cir. 2005); *see also, e.g.*, *Brock*, 874 F.2d at 311 ("the most useful and conclusive type of evidence . . . is epidemiological studies"); *Perry v. Novartis Pharms. Corp.*, 564 F. Supp. 2d 452, 465 (E.D. Pa. 2008) ("no reliable scientific approach can simply ignore the epidemiology that exists").

Dr. Glass's general causation opinion is unreliable for precisely the same reasons. He has ignored an extensive body of evidence—indeed, the best available evidence—which demonstrates exactly the opposite conclusion to the one he seeks to present at trial. Accordingly, Dr. Glass's general causation opinion should be excluded.

2. The Fergusson Study Does Not Support Dr. Glass's General Causation Opinion

Against FDA's analysis of controlled clinical trial data and the results of numerous published epidemiological studies finding no increased risk of suicide in adult patients, a single epidemiological study purported to find an increased risk of suicidality in adult patients—not in patients treated with sertraline, specifically, but for a broader grouping of medications. *See*

[10] The *Rimbert* court further noted that "[t]here are numerous peer-reviewed publications on controlled clinical trials, meta-analyses of controlled clinical trials, and other epidemiological studies that support the proposition that Prozac and other SSRIs are not associated with suicidality or violent behavior." 2009 WL 2208570, at *13. As shown in this brief, as well as the report of Dr. Gibbons (Ex. 10), the same is true for sertraline.

D. Fergusson et al., *Association Between Suicide Attempts and Selective Serotonin Reuptake Inhibitors: Systematic Review of Randomised Controlled Trials*, 330 BMJ 396 (2005) (the "Fergusson study") (Ex. 11). This study fails to support Dr. Glass's opinions for several reasons. ***First***, the Fergusson study analyzed several distinct medications together as a group. *See id.* at 1 (noting that study purports to find an "association between suicide attempts and the use of SSRIs"); (Glass Dep. at 11:7-17.) As such, the Fergusson study expressed no finding whatsoever as to sertraline itself, much less any finding that sertraline itself can cause suicide or suicide attempts. And it is well settled that an expert may not reliably extrapolate from data concerning a group of medications or chemical compounds to express a causation opinion as to a specific medication or compound. *See, e.g.*, *Wells v. Smithkline Beecham Corp.*, 601 F.3d 375, 380 (5th Cir. 2010) (finding that study could not support general causation because it "represented a class association, as opposed to a specific medication, finding"); *Knight v. Kirby Inland Marine Inc.*, 482 F.3d 347, 353 (5th Cir. 2007) (finding that study could not support general causation because the "study focused on organic solvents as a class, including a wide-range of chemicals to which appellants were never exposed").[11]

[11] Nor does the fact that SSRIs as a class have certain similarities in their mechanism of action justify extrapolation of causation based on class data, or data concerning other SSRIs. *See, e.g., Richardson v. Richardson-Merrell, Inc.*, 857 F.2d 823, 830 (D.C. Cir. 1988) (even for drugs with similar chemical structures, extrapolation from effects of one compound to another could not by itself furnish sufficient foundation for conclusion that drug at issue caused claimed effects); *Grimes v. Hoffman-LaRoche, Inc.*, 907 F. Supp. 33, 38 & n.11 (D.N.H. 1995) (testimony unreliable where expert failed to show "any scientifically reliable basis for concluding Accutane causes cataracts simply because other photosensitive drugs cause cataracts"); *Lynch v. Merrell-Nat'l Labs*, 646 F. Supp. 856, 866 (D. Mass. 1986) (where plaintiffs witnesses admitted that "chemically analogous" drugs differed "in some respects from Bendictin . . . and that these differences may affect its properties", testimony did not comport with Rule 703 requirement that expert's opinion "be grounded on facts or data of a type reasonably relied upon by experts in the particular field"), *aff'd*, 830 F.2d 1190 (1st Cir. 1987).

Second, as the FDA has recognized, the Fergusson study was subject to serious limitations due to a lack of information available to the study authors. Commenting on the Fergusson study, FDA has noted that "[t]here were serious limitations to this review, most important being a lack of any information on adverse events for 58% of the patients eligible for the analysis." (*See* Nov. 16, 2006 Mem. by Mr. T. Laughren, Director of FDA Division of Psychiatry Products at 4, Ex. 12.) Specifically comparing Fergusson to its own analysis, FDA has commented that "the Fergusson paper includes many fewer subjects than are obtained in this review, probably due to its limitation to public data." (*See* Stone and Jones at 41.)

Third, the reliability of the Fergusson paper has been called into question by errors in the odds ratio calculations provided in the original publication. Fergusson and colleagues have acknowledged at least one error in the calculated odds ratios for their study. (*See* Correction to *Association Between Suicide Attempts and Selective Serotonin Reuptake Inhibitors: Systematic Review of Randomized Controlled Trials*, Ex. 13.) Other calculated odds ratios in the Fergusson paper also have been called into question. (*See* A. Mitchell, *Do Selective Serotonin Reuptake Inhibitors Cause Suicide?: Data Seem to be Incorrect*, Ltr. Published in BMJ 5/12/05.)[12]

No legitimate science would make this same illogical leap, and courts exclude testimony of those who try to do so:

> "The problem with these extrapolations is that they depend on numerous logical shortcuts and inferential leaps. . . . Without testing, epidemiological study, or controlled experimentation, these theories constitute no more than scientific speculation and cannot be admitted as reliable scientific knowledge."

Nelson v. American Home Prods. Corp., 92 F. Supp. 2d 954, 972 (W.D. Mo. 2000) (emphasis added) (citation omitted) (footnote omitted).

[12] Available at http://www.bmj.com/content/330/7500/1149.3.full?sid=328e472d-7d0a-4362-93da-722aa31b4bed.

II. DR. GLASS'S SPECIFIC CAUSATION OPINION IS UNRELIABLE BECAUSE HE KNOWS ALMOST NONE OF THE FACTS OF THIS CASE

Dr. Glass ultimately admits—as he must give the body of evidence discussed above—that SSRIs ***reduce*** the risk of suicide in the majority of patients:

> Q. And then, under Interpretation, do you see, "Based on data from observational studies, use of SSRIs may be associated with a reduced risk of suicide in adults with depression?"
>
> A. Yes.
>
> Q. And you were not aware of the study before today?
>
> A. But I believe that it's true. I think that SSRIs do reduce the risk of suicide in a majority of patients, but not all of them.

(Glass Dep. at 238:14-239:1.) Dr. Glass's opinion concerning Roberts is thus that, despite the fact that sertraline reduces suicide risk in most patients, it actually caused Roberts' actions because she fell within a small subgroup of patients for whom the risk is increased. (*Id.* at 158:17-160:15.)

As an initial matter, Dr. Glass's opinion that such a small subgroup of patients exists is completely unreliable. As Dr. Glass readily admits, there is no scientific support for the existence of such a subgroup aside from anecdotal case reports:

> Q. Is there anything that establishes the existence of the small subgroup aside from case reports?
>
> A. No. . . .

(*Id.* at 160:16-19.) As courts have routinely held, such uncontrolled, anecdotal evidence cannot provide reliable evidence of causation. *See Newton v. Roche Labs. Inc.*, 243 F. Supp. 2d 672, 680 & n.11 (W.D. Tex. 2002) (noting that the "Fifth Circuit and many other courts have soundly rejected case reports as an acceptable basis for causation" and collecting cases so holding);

Havner, 953 S.W.2d at 720 (noting that FDA regulations "state that '[i]solated case reports, random experience, and reports lacking the details which permit scientific evaluation will not be considered'" and that "courts should likewise reject such evidence because it is not scientifically reliable"). In summary, Dr. Glass admits that SSRIs such as sertraline ***decrease suicide risk,*** rather than cause suicide, in "a majority of patients," but claims that the opposite purported effect occurs in some "small subgroup" of patients that he cannot identify and the existence of which he admits is based on nothing more than speculation from anecdotal case reports.

Even leaving this inadequacy aside, however, Dr. Glass's specific causation opinion still would not be reliable because Dr. Glass rendered the opinion in nearly complete ignorance of the facts of this case. Dr. Glass admitted at his deposition that he has not read ***any*** of the fourteen depositions that have been taken of Roberts' family, friends and medical providers. (Glass Dep. at 68:19-21.) As Dr. Glass described his specific causation opinion, it was based primarily on a conclusion that Roberts exhibited a "dramatic change in behavior" after she began using sertraline. (*See* Glass Rpt. at 8, Ex. 2.) This is classic, unscientific, *post hoc* reasoning. And yet Dr. Glass elected not to review any of the available evidence concerning Roberts' behavior before or after her sertraline use.

For example, Dr. Glass makes much of the fact that Roberts purportedly acted in an "agitated" manner after she used sertraline. (Glass Rpt. at 8.) But, because he did not review any depositions, Dr. Glass was not aware that Roberts' treating gynecologist, Dr. Gupta, testified that Roberts began acting in an uncharacteristic and agitated manner beginning in June 2007, more than one month ***before*** she ingested sertraline for the first time. (*See* Glass Dep. at 183:22-186:12.) Dr. Glass also was not aware that two other witnesses testified at deposition that

Roberts acted in a "frantic" manner in the weeks ***before*** she took sertraline. (*Id.* at 218:12-221:8.) Nor was he aware that one of Roberts' friends spoke with her about her use of sertraline and that Roberts told that friend that she was not experiencing any adverse effect from Zoloft, but rather "couldn't tell any difference" in the way she felt while using sertraline. (*Id*. at 212:13-214:2.) Dr. Glass also did not know that Roberts spoke with another friend the day before she died and that she seemed "very normal" during that conversation. (*Id.* at 216:14-217:21.)

In sum, Dr. Glass's total disregard for the facts leads him to incomplete and demonstrably false conclusions. His specific causation opinion is both lacking in sufficient supporting data and based on incorrect assumptions, and is, accordingly, unreliable. *See*, *e.g.*, *General Electric Co. v. Joiner* 522 U.S. 136, 146 (1997) ("nothing in either *Daubert* or the Federal Rules of Evidence requires a district court to admit opinion evidence that is connected to existing data only by the *ipse dixit* of the expert")*; Guillory v. Domtar Industries Inc.*, 95 F.3d 1320, 1331 (5th Cir.1996) ("Expert evidence based on a fictitious set of facts is just as unreliable as evidence based upon no research at all. Both analyses result in pure speculation."); *Allen v. Pennsylvania Engineering Corp.*, 102 F.3d 194, 199 (5th Cir.1996) (expert's opinions inadmissible where their "background information concerning [plaintiff]'s exposure to [the toxic substance at issue] is so sadly lacking as to be mere guesswork").

III. DR. GLASS'S OPINIONS CONCERNING SUPPOSED DELAY AND MINIMIZATION BY PFIZER ARE PURE SPECULATION

The final opinion offered in Dr. Glass's report is that "the Pharmaceutical Manufacturer, in this case Pfizer, attempted to minimize those particular side effects, and delay as long as possible notifying physicians and the FDA of them." (Glass Rpt. at 9.) Dr. Glass admitted, however, that this "opinion" is not based on review or knowledge concerning any document or

action by Pfizer. (Glass Dep. at 121:23-122:22; 124:4-7; 232:4-13.) Accordingly, this opinion is nothing other than "subjective belief or unsupported speculation" and should be excluded. *Daubert*, 509 U.S. at 579, 590.

CONCLUSION

For the reasons set forth above, the Court should exclude the testimony and report of Dr. Glass.

Dated: December 27, 2011

Respectfully submitted,

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CERTIFICATE OF SERVICE (CM/ECF)

I HEREBY CERTIFY that a true and correct copy of DEFENDANTS' MOTION TO EXCLUDE TESTIMONY AND REPORT OF GEORGE GLASS, M.D. was served via manner indicated below this 27 day of December, 2011 to the following:

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s/ Andrew Myers

CERTIFICATE OF CONFERENCE

Counsel has complied with the meet and confer requirement in Local Rule CV-7(h) and this motion is opposed. The personal conference required by Rule CV-7 was conducted on December 27, 2011 via telephone between Andrew Myers, attorney for Defendants, and Jessica Graham, attorney for Plaintiffs, and no agreement could be reached because there is a disagreement over the relevance and admissibility Dr. Glass's testimony. Discussions have ended in an impasse leaving an open issue for the Court to resolve.

Signed: s/ Andrew Myers
Andrew Myers